APPENDIX C

LUNG CANCER MORTALITY RATES ATTRIBUTABLE TO SPOUSAL ETS IN INDIVIDUAL EPIDEMIOLOGIC STUDIES

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Many of the epidemiologic studies on lung cancer and environmental tobacco smoke (ETS) were part of larger investigations that included ever-smokers and never-smokers. For those studies, the lung cancer mortality rate (LCMR) for all causes, appropriate to the location and time period of the study, has been obtained from other sources. Those values and parameter estimates from the studies are used to partition the excess LCMR from all causes (i.e., the excess after allowance for baseline sources) into components attributable to ever-smokers (from current and former smoking) and never-smokers (from exposure to spousal ETS) and to estimate the LCMR in the subpopulations of interest--unexposed never-smokers (meaning not exposed to spousal smoking), exposed never-smokers (exposed to spousal smoking), and ever-smokers ("exposed" is not used to mean exposure to nonspousal ETS, which applies to the whole target population). The method is explained in Sections 6.3.1 and 6.3.2.

Lung cancer mortality rates for the case-accrual periods of case-control studies are displayed in Table C-1

Table C-1. Female lung cancer mortality from all causes in case-control studies[1]

Study	Location	Case accrual	Begin	Average	End	Accrual-10 yrs average[2]	Accrual-20 yrs average[2]
AKIB	Japan	1971-80	5.13	6.05	7.08	4.57	2.30
BROW	USA	1979-82	15.68	17.29	19.09	9.49	4.75
BUFF	USA	1976-80	13.94	15.29	17.20	7.86	4.38
CHAN	HK	1976-77	23.59	23.59	23.59	19.05	*
CORR[3]	USA	1979-82	26.0	26.0	26.0	9.49	4.75
GAO[4]	China	1984-86	*	18.0	*	14.3[3]	5.1[3]
GARF	USA	1971-81	9.45	13.55	17.20	6.87	*
GENG[4]	China	1983	*	27.8	*	13.8[3]	*
HIRA[5]	Japan	1965-81	4.46	5.70	7.08	4.01	*
HUMB[3]	USA	1980-84	17.7	17.7	*	10.55	5.13
INOU	Japan	1973-83	5.55	6.53	7.46	4.93	2.95
JANE[3]	USA	1982-84	23.7	23.7	*	9.06	5.42
KABA[6]	USA	1961-80	4.69	13.20	17.20	6.61	4.16
KALA[6]	Greece	1987-89	6.58	6.58[6]	6.58	6.75	5.83[6]
KATA[6]	Japan	1984-87	*	7.46[6]	*	4.66	2.26
KOO	HK	1981-83	22.34	22.61	22.75	19.82	*
LAMT[6]	HK	1983-86	22.75	23.46	23.69	21.33	*
LAMW	HK	1981-84	22.34	22.88	23.69	20.09	*
LEE	Eng/Wal	1979-82	16.28	17.11	17.89	12.60	8.1
PERS[6]	Sweden	1961-80	3.71	5.09	7.56	3.95[6]	*
SHIM[6]	Japan	1982-85	7.46	7.46[6]	7.46	5.65	4.28
SOBU[6]	Japan	1986-88	7.46	7.46[6]	7.46	6.36	4.93
SVEN[6]	Sweden	1983-85	7.72	7.72[6]	7.72	5.78	3.80
TRIC	Greece	1978-80	6.88	6.40	5.99	5.75	5.31[7]
WU	USA	1981-82	17.20	18.15	19.09	10.14	4.96
WUWI[8]	China	1985-87	*	11.6	*	9.2[2]	*

[1]Rates are per 100,000 per year, standardized to the 1950 world population age distribution. Data are drawn from Kurihara et al. (1989), and annual rates for 2-year periods were averaged over the years cases were accrued for each study unless otherwise noted. Where part (or all) of the accrual period fell 1 or 2 years outside the years for which rates were available, rates from the nearest 2-year period available were assumed to apply to the missing years. U.S. rates are for white females only.

(continued on the following page)

[2]The accrual-10 years average is the average for the time period of the same length as the accrual period but 10 years previous to it. Similarly, the accrual-20 years value is for the time period 20 years previous to the accrual period.

[3]Data for accrual period from 1978-82 rates in IARC (1987b), standardized to 1950 world population from Kurihara et al. (1989). For Correa, weighted average of white and black rates; for Humble, weighted average of Hispanic and non-Hispanic white rates.

[4]Accrual period data for GAO and GENG derived from IARC (1987b) by standardizing to same 1950 world population used by Kurihara et al. (1989). GAO rates are for 1978-82; GENG, 1981-82. For the accrual-10 years value, GAO and GENG are 1973-75 rates standardized to the 1960 world population from China Map Press (1979). The GAO accrual-20 years value is nonadjusted 1961 rate from Kaplan and Tsuchitani (1978).

[5]The nested case-control study of Hirayama (mortality rates for this study also apply to the cohort study in which it is nested).

[6]Where rates for the period were not available in Kurihara et al. (1989), substitutions were made as follows: Kalandidi from 1984-85 rates; Kabat, 1982-83; Katada, 1982-83; Lam, T., 1984-85; Pershagen, 1952-53; Shimizu, 1982-83; Sobue, 1982-83; and Svensson, 1982-83.

[7]World-standardized rate for 1961-65 from Katsouyanni et al. (1990) (in Greek: translation provided by Trichopoulos).

[8]Accrual period value estimated by multiplying LCMR in Shanghai for period 1978-82 (standardized to the 1950 world population) by the ratio of LCMRs in Liaoning and Heilonjiang to Shanghai, for the period 1973-75 (standardized to the 1960 world population). Data are from China Map Press (1979). Value for accrual-10 years is the 1973-75 rate.

*Data not available.

. For the studies that collected data on both ever-smokers and never-smokers, the parameter estimates used are shown in Table C-2

Table C-2. Parameter values used to partition female lung cancer mortality into component sources[1]

Case-control	Lung cancer mortality	Ever-smokers		Never-smokers	
		Prevalence (%)	Relative risk	Percentage exposed (%)	Relative risk
AKIB	6.05	21	2.38	70	1.50
BROW	17.29	29	4.30	15	1.50
BUFF	15.29	59	7.06	84	0.81
CHAN	23.59	26	3.48	47	0.74
CORR	26.00	47	12.40	46	1.90
GAO	18.00	18	2.54	74	1.19
GARF(Coh)	7.00[2]	33	3.58	72	1.15
GENG	27.80	41	2.77	44	2.16
HIRA	5.70	16	3.20	77	1.53
HIRA(Coh)	5.70[2]	16	3.20	77	1.37
HUMB	17.70	41	16.30	56	1.98
INOU	6.53	16	1.66	64	2.55
KABA	13.20	42	5.90	60	0.74
KALA	6.58	17	3.32	60	1.92
KOO	22.61	32	2.77	49	1.54
LAMT	23.46	24	3.77	45	1.64
LAMW	22.88	22	4.12	56	2.51
LEE	17.11	60	4.61	68	1.01
SOBU	7.46	21	2.81	54	1.13
SVEN	7.72	43	5.97	66	1.19
TRIC	6.40	11	2.81	52	2.08
WU	18.15	58	4.38	60	1.31
WUWI	11.60	37	2.24	55	0.78

[1]For studies with data on both ever-smokers and never-smokers. Table entries are drawn from Tables 5-8, B-11, and C-1, which contain explanatory footnotes.
[2]Average of world-standardized rates for location during followup period of study from Kurihara et al. (1989). White female rates used for GARF.

. The value for the lung cancer mortality rate is from Table C-1, and the remaining estimates are from individual study data. The rate for the followup period of the study is estimated for HIRA(Coh) and GARF(Coh). These values may not be very "representative" for lung cancer mortality in these two cohort studies because they extended over several years, and the LCMRs changed from year to year, particularly in the United States. This same difficulty arises in choosing a "representative" year for lung cancer mortality in the case-control studies, although to a lesser degree. The most extreme examples are KABA, PERS, INOU, and GARF, with case-accrual periods of 10 years or more.

The estimates of prevalence of ever-smokers and the percentage of never-smokers exposed to spousal smoking are the observed proportions in the control group. The extent to which the control group is representative of the country's population differs between studies; the study reviews in Appendix A provide more detailed information. The restriction of cell types among cases in some studies is another consideration. Active smoking is much more strongly associated with occurrence of squamous and small cell carcinoma than with large cell carcinoma and adenocarcinoma. FONT presents evidence that passive smoking is more associated with adenocarcinoma than with other cell types. As noted in Table 5-14, some studies excluded candidate lung cancer cases of specific histopathological types. This may produce some bias and distortion of comparison between studies. For example, BROW includes only cases of adenocarcinoma, which should bias the relative risk of ever-smokers toward unity, thus

attributing too little lung cancer mortality to active smoking and too much to passive smoking and background sources.

Of a more positive nature, there is some advantage to using data from a single study to assign attributable *fractions* to different causes. To estimate the yearly number of lung cancers from each cause, the fraction is multiplied by the LCMR for the location and time of the study; that figure has to be obtained from sources on vital statistics. As seen in Table C-2, the mortality rates from lung cancer vary considerably between and within countries. For example, the rates used for studies in the United States range between 9 and 26. Applying the lung cancer rate suitable to each individual study should provide better estimates for comparison within a country than using a single figure for the whole country for some specific year.

Despite the reservations described, partitioning the lung cancer mortality for each study into components attributable to ever-smoking, spousal ETS, and baseline sources (nontobacco smoke and nonspousal ETS) provides a broad overview worth noting. The calculated values are shown in Table C-3

Table C-3. Female lung cancer mortality rates by attributable source[1]

		Baseline sources[2]		Spousal smoking		Ever-smoking	
Study	Location	No.	%	No.	%	No.	%
AKIB	Japan	3.47	57	0.96	16	1.61	27
BROW	USA	8.22	48	0.44	3	8.63	50
BUFF	USA	3.34	22	0.00	0	11.95	78
CHAN	HK	14.34	61	0.00	0	9.25	39
CORR	USA	2.89	11	0.63	2	22.47	86
GAO	China	12.36	69	1.42	8	4.22	23
GARF(Coh)	USA	3.41	49	0.25	4	3.34	47
GENG	China	10.67	38	3.21	12	13.92	50
HIRA(Coh)	Japan	3.28	58	0.78	14	1.63	29
HUMB	USA	1.57	9	0.51	3	15.62	88
INOU	Japan	2.97	45	2.47	38	1.09	17
KABA	USA	4.32	33	0.00	0	8.88	67
KALA	Greece	3.04	46	1.39	21	2.15	33
KOO	HK	11.41	50	2.05	9	9.14	40
LAMT	HK	10.94	47	2.39	10	10.12	43
LAMW	HK	7.35	32	4.85	21	10.68	47
LEE	Eng./Wales	5.37	31	0.01	0	11.73	69
SOBU	Japan	5.05	68	0.28	4	2.13	29
SVEN	Sweden	2.19	28	0.16	2	5.37	70
TRIC	Greece	3.42	53	1.71	27	1.27	20
WU	USA	5.17	28	0.40	2	12.58	69
WUWI	China	7.95	69	0.00	0	3.65	31

[1]Rates are per 100,000 per year. Data not available for GARF, JANE, PERS, SHIM, BUTL(Coh), and HOLE(Coh).
[2]Nonspousal ETS and non-ETS sources.

. Estimates of relative risk for exposure to spousal ETS (RR_2 in notation of Section 6.3.2) less than 1.0 (see Table 5-9) were replaced by 1.0 to avoid a negative LCMR attributable to spousal ETS and the consequent inflation of the LCMR attributable to baseline sources and ever-smoking. Aside from the studies for Hong Kong and China, estimates of lung cancer mortality due to background sources cluster in the interval 1.5 to 5.5 (excluding BROW, which is strongly biased), predominantly from 3 to 5. The values for Hong Kong and China, however, are much higher, ranging from 7 to 14.5. The presence of indoor sources of non-ETS encountered in some of the studies in China may be a factor, but there is no apparent explanation for the outcome in Hong Kong. Assuming that the background rate of lung cancer is much higher in Hong Kong (and possibly China) as it appears, then the question arises as to whether the high excess rate relative to other countries may be attributable to higher exposure to ETS aside from spousal smoking or whether it is more likely due to other causes. Summary data from the 10-country collaborative study of ETS exposure to nonsmoking women conducted by the International Agency for Research on Cancer (IARC) (Riboli et al., 1990) was kindly submitted to us for Hong Kong, Japan (Sendai), and the United States (Los Angeles, New Orleans) from Drs. L.C. Koo, H. Shimizu, A. Wu-Williams, and T.H. Fontham, respectively. The average cotinine/creatinine (ng/mg) levels for nonsmoking women who are not employed and not married to a smoker are close for Sendai, Los Angeles, and New Orleans, but they are several times higher for Hong Kong. Consequently, a high contribution to background lung cancer mortality from ETS aside from spousal smoking cannot be eliminated as a factor.

The lung cancer attributable to ever-smoking, spousal smoking, and baseline sources depends on the population proportions for those categories as well as the relative risks. Study estimates of the LCMR in each category, in units of lung cancer deaths per 100,000 at risk per year, are shown in Table C-4

Table C-4. Lung cancer mortality rates of female ever-smokers (ES) and never-smokers (NS) by exposure status[1]

Study	Location	(1) Unexposed NS[2]	(2) ExposedNS[3]	(3) ES	(2) As a percentage of (3)	(2) - (1) As a percentage of (3) - (1)
AKIB	Japan	3.47	5.21	11.16	47	23
BROW	USA	8.21	12.32	37.99	32	14
BUFF	USA	3.34	3.34	23.59	14	0
CHAN	HK	14.34	14.34	49.91	29	0
CORR	USA	2.89	5.49	50.70	11	5
GAO	China	12.35	14.70	35.79	41	10
GARF(Coh)	USA	3.41	3.92	13.54	29	5
GENG	China	10.66	23.03	44.62	52	36
HIRA(Coh)	Japan	3.28	4.49	13.49	33	12
HUMB	USA	1.57	3.11	39.66	8	4
INOU	Japan	2.96	7.56	9.80	77	67
KABA	USA	4.32	3.78	25.46	17	0
KALA	Greece	3.04	5.84	15.66	37	22
KOO	HK	11.41	17.57	39.98	44	22
LAMT	HK	10.94	17.94	53.12	34	17
LAMW	HK	7.35	18.45	55.89	33	23
LEE	Eng/Wal	5.36	5.42	24.91	22	0
SOBU	Japan	5.05	5.70	15.18	38	6
SVEN	Sweden	2.18	2.60	14.69	18	3
TRIC	Greece	3.41	7.10	14.99	47	32
WU	USA	5.16	6.77	26.85	25	7
WUWI	China	7.95	7.95	17.81	45	0

[1]Rates are per 100,000 per year. Data not available for GARF, JANE, PERS, SHIM, BUTL(Coh), and HOLE(Coh).
[2]Exposed to baseline sources--nonspousal ETS and non-ETS sources.
[3]Exposed to baseline sources plus spousal ETS.

. The last two columns show the ratios of the LCMR and the excess LCMR for exposed never-smokers to ever-smokers. As above, relative risk estimates of less than 1.0 were set to 1.0 for the calculations. There is considerable variability across study estimates, even within the same country, as observed previously in the relative risks for spousal smoking.

To summarize, for studies that included data on ever-smokers, the LCMR for all causes was partitioned by attributable source (Table C-3). Although there is considerable uncertainty in the estimates from statistical variability and other sources, the outcomes provide some useful gross comparisons. For example, the lung cancer mortality rates from all causes differ markedly between countries and also vary widely between studies within the United States. The proportion of lung cancers attributable to ever-smoking is very high in the United States, compared with some more traditional countries (e.g., Japan and Greece).

Individual study estimates of the number of lung cancer deaths per year per 100,000 of the female population from exposure of never-smokers to spousal ETS are predominantly between 0 and about 2.5. Estimates of the LCMR attributable to baseline sources (nonspousal ETS and nonsmoking causes) are somewhat higher, largely between 2 and 5, except in Hong Kong and China, where they range between 7+ and 14. (The U. S. study denoted as BROW has a high value, but that should be upwardly biased because it used only cases of adenocarcinoma, which is not a common cell type in smokers.) For reasons discussed in Chapter 5, we would be reluctant to draw conclusions about China on the basis of the epidemiologic studies. The evidence from Hong Kong, however, is very suggestive that the lung cancer rate in women due to baseline sources is very high. The extent to which that is attributable to nonsmoking sources of lung cancer and/or high exposure to nonspousal ETS is not apparent. The cotinine data for Hong Kong from the 10-country IARC study (Riboli et al., 1990) is consistent with excessively high ETS exposure; therefore, nonspousal ETS may be a factor.